



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

MW

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/058,825 | 01/30/2002 | Roderick John Scott | 11696-067001 | 2437 |

26191 7590 09/11/2007
FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

| EXAMINER | |
|----------------|--|
| BAUM, STUART F | |

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1638 | |

| MAIL DATE | DELIVERY MODE |
|------------|---------------|
| 09/11/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/058,825
Filing Date: January 30, 2002
Appellant(s): SCOTT, RODERICK JOHN

MAILED
SEP 11 2007
GROUP 1600

Ronald C. Lundquist
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/5/2007 appealing from the Office action mailed 10/19/2006.

Art Unit: 1638

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

Art Unit: 1638

(8) Evidence Relied Upon

Finnegan et al., Nucleic Acids Res. 23:2383-2388 (1993)

Jacobsen et al (2000, Current Biology 10:179-186)

Gutterson (1995, HortScience 30(5):964-966)

Emery et al (2003, Current Biology 13:1768-1774)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-21, 62-67, 69, 71, 76-78, and 80-93 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claim 20 is indefinite in the recitation "a sequence whose transcription product comprises a partial or full length *Arabidopsis* DNA methyltransferase 1 (Met1) sequence." Appellant has disclosed "Therefore, the designation *Arabidopsis* Met1 sequence will always refer to the sequence of Accession No. L10692..." (page 13 of Remarks filed 11/7/2005, 1st full paragraph). Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence. One skilled in the art knows transcription products are RNA molecules that may comprise non-translated regions, i.e., introns and 5' and 3' non-

Art Unit: 1638

translated regions. In addition, the transcription product would be a mRNA molecule that is in reverse orientation from the strand from which it was transcribed. Therefore, the transcription product would not have the same sequence as the DNA sequence disclosed in Accession No. L10692. Claim 62 is indefinite in the recitation “a sequence whose transcription product comprises a partial or full length *Zea mays* sequence orthologous to the *Arabidopsis* methyltransferase 1 (Met1) sequence.” Appellant has disclosed “Therefore, the designation *Arabidopsis* Met1 sequence will always refer to the sequence of Accession No. L10692...” (page 13 of Remarks filed 11/7/2005, 1st full paragraph). Said sequence is a DNA sequence, therefore, it is unclear how a transcription product can be a DNA sequence and not a mRNA sequence. One skilled in the art knows transcription products are RNA molecules that may comprise non-translated regions, i.e., introns and 5' and 3' non-translated regions. In addition, the transcription product would be a mRNA molecule that is in reverse orientation from the strand from which it was transcribed. Therefore, the transcription product would not have the same sequence as the DNA sequence disclosed in Accession No. L10692, for the reasons state above and because Accession No. L10692 is the *Arabidopsis* sequence and not the *Zea mays* sequence.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 20-21, 62-67, 69, 71, 76-78, 80-93 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

Art Unit: 1638

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for the production of modified endosperm comprising a sequence whose transcription product comprises a partial *Arabidopsis* DNA methyltransferase 1 (Met1) sequence or a partial *Zea mays* sequence orthologous to the *Arabidopsis* Met1 sequence, or wherein the transcription product comprises an antisense or sense nucleic acid copy of the *Zea mays* or *Arabidopsis* partial or full-length sequence, or wherein the transcription product is a partial sense copy of the *Zea mays* or *Arabidopsis* sequence.

The Examiner interprets “an antisense or sense nucleic acid copy” to read on any size antisense or sense sequence.

Appellant discloses subcloning the MET1 cDNA, which is 4.7kb long, isolated by RT-PCR from an *Arabidopsis* cDNA library using the MET1F primer of SEQ ID NO:5 and MET1R primer of SEQ ID NO:6 (page 30, Example 3).

Appellant does not disclose any sequence whose transcription product is a partial *Arabidopsis* Met1 or *Zea mays* orthologous sequence to the *Arabidopsis* Met1 sequence. Appellant does not identify essential regions of the *Arabidopsis* Met1 sequence, nor any partial sequences thereof, nor any partial sequence of the *Zea mays* orthologue of the *Arabidopsis* Met1 sequence, that can be used to down-regulate one or more methylating enzymes present in a plant.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the

Art Unit: 1638

structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Appellant fails to describe a representative number of sequences whose transcription product is a partial sequence of the *Arabidopsis* Met1 sequence, or partial sequences of the *Zea mays* homologue of the *Arabidopsis* Met1 sequence, that can be used to down-regulate one or more methylating enzymes in any plant. Furthermore, Appellant fails to describe structural features common to members of the claimed genus of polynucleotides. Hence, Appellant fails to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements of said sequences that can be used to down-regulate any methylating enzyme in any plant, it remains unclear what features identify an *Arabidopsis* Met1 sequence or identify the *Zea mays* homologue of the *Arabidopsis* Met1 sequence, or what sequences can be used to identify partial sequences of the *Arabidopsis* Met1 or partial sequences of the *Zea mays* homologue of the *Arabidopsis* Met1 sequence. Since the genus of said sequences has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Scope of Enablement

Claims 20-21, 62-67, 69, 71, 76-78, 80-93 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for increasing the amount of endosperm in an *Arabidopsis* or *Brassica* seed or increasing the weight of an *Arabidopsis* or *Brassica* seed comprising a construct comprising a full length MET1 DNA sequence operably linked to the AGL5 promoter, wherein the sequence is in antisense orientation, or wherein the MET1 DNA sequence is isolated by RT-PCR from *Arabidopsis* using the primers MET1F of SEQ ID NO:5 and MET1R of SEQ ID NO:6 and *Arabidopsis* and *Brassica* plant transformation therewith, does not reasonably provide enablement for claims broadly drawn to a method of modifying the endosperm from any plant comprising down-regulating any DNA methylating enzyme using a sequence whose transcription product comprises a partial or full length *Arabidopsis* Met1 sequence or which comprises a partial or full-length *Zea mays* sequence orthologous to the *Arabidopsis* Met1 sequence, or wherein the nucleic acid is a partial or full length sequence in sense or antisense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or

Art Unit: 1638

absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method for the production of modified endosperm in part comprising a transcription product comprising a partial or full-length *Arabidopsis* DNA methyltransferase 1 (Met1) sequence or a partial or full-length *Zea mays* sequence orthologous to the *Arabidopsis* Met1 sequence, or wherein the transcription product comprises an antisense nucleic acid, or wherein the transcription product is a sense copy of the *Zea mays* or *Arabidopsis* sequence, or wherein the transcription product is a partial sense copy of the *Zea mays* or *Arabidopsis* sequence.

Appellant discloses cloning a sequence that encodes the *Arabidopsis* MET1 protein, wherein the nucleic acid sequence is 4.7kb long, in which the sequence was isolated by RT-PCR from an *Arabidopsis* cDNA library using the MET1F primer of SEQ ID NO:5 and MET1R primer of SEQ ID NO:6. Appellant discloses subcloning the nucleic acid sequence into a vector comprising the AGL5 or AP3 promoter in antisense orientation (page 30, Example 3; and Figures 6 and 7) and *Arabidopsis*, *Brassica campestris* and *Brassica oleraceae* transformation therewith (page 31, Example 4, page 33, Example 5). Plants expressing the pAGL5Met1as construct produced seed with increased weight (page 31, lines 26-28). Appellant discloses the mean seed weight of plants transformed with pAP3Met1as is less than that of 2x-2x seed (page 32, lines 21-22). Appellant discloses the mean seed weight of 2x-2x seed is 22 micrograms (page 31, lines 26-28). Appellant states "pAGL5Met1as and pAP3Met1as were transformed into *Brassica campestris* and *Brassica oleraceae* via standard methods. Reciprocal crosses between

Art Unit: 1638

the transgenic individuals of the two species yield plump seeds which germinate to give hybrid plants. Crosses between wild type individuals of the two species result in shriveled seeds which fail to germinate. Hence the two transgenes overcome the normal barrier to interspecific hybridization” (page 33, lines 16-21).

Re: claims 20 and 62 recite “the nucleic acid molecule comprising a promoter ... and a sequence whose transcription product...”. As written, the Examiner broadly interprets the claim to mean a construct comprising a promoter and another sequence, wherein the sequence is located in a position not necessarily next to the promoter. Therefore, the promoter would not affect the transcription of the sequence. Given this interpretation of the claim, the method is not enabled because it is unclear how the sequence can be transcribed at the appropriate time and in the appropriate cells.

Claims 20 and 62 recite that the nucleic acids are effective for down-regulating one or more DNA methylating enzymes present in the plant, whereby the degree of DNA methylation of nucleic acid in the plant is reduced.... The state-of-the-art teaches down-regulating methylating genes produces unpredictable results. Jacobsen et al (2000, Current Biology 10:179-186) teach transforming *Arabidopsis* with a nucleic acid encoding the MET1 protein operably linked to a promoter in antisense orientation caused a decrease in methylation by 80%-90%. Jacobsen et al disclose that “Surprisingly, this work showed that the floral development gene *SUPERMAN* was ectopically *hypermethylated* [emphasis added] and silenced” (page 180, left column, 1st full paragraph).

The Examiner interprets the recitation “comprises a partial ...sequence” to read on a great number of sequences because a partial sequence reads on any two nucleotides from

Art Unit: 1638

Appellant's Met1 sequence. Appellant has only disclosed primer sequences to be used for isolating the full length *Arabidopsis* MET1 sequence from an *Arabidopsis* cDNA library (See pages 30-31, Example 3a). Appellant has not disclosed how one makes or isolates any of the other sequences that are encompassed by Appellant's broad claims. Appellant has not taught which regions of the respective polynucleotides can be used to amplify, for example, the *Zea mays* orthologous sequence, or which regions can be used as a probe to isolate any of said polynucleotide sequences whose transcription product comprises a partial *Arabidopsis* or *Zea mays* Met1 sequence that is effective for downregulating one or more DNA methylating enzymes present in the plant and produce a plant whose seeds produce modified endosperm.

Appellant's claims are drawn to a method comprising the *Arabidopsis* Met1 sequence or the *Zea mays* homologue of the *Arabidopsis* Met 1 sequence, both of which are used to down regulate any methylating enzyme from any plant. In other words, using heterologous sequences to down regulate endogenous genes. Using DNA sequences to reduce expression of the endogenous corresponding gene through the mechanism of sense suppression produces unpredictable results. Gutterson (1995, HortScience 30(5):964-966) teaches that the chrysanthemum and petunia chalcone synthase (CHS) genes are 70% identical to each other, and that transforming petunia plants with the chrysanthemum CHS gene did not co-suppress the endogenous petunia CHS gene (page 965, left column, second paragraph). Gutterson reports similar data using another petunia gene in the anthocyanin pathway.

The state-of-the-art teaches that antisense molecules that exhibit less than 100% sequence identity to the target sequence produce unexpected results. Emery et al (2003, Current Biology 13:1768-1774) disclose experiments in which a target sequence of a micro-RNA was changed by

Art Unit: 1638

two base-pairs. The altered base-pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence's encoded protein (page 1769, right column, 2nd full paragraph).

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of a nucleic acid encoding the *Arabidopsis* Met1 protein as probes or by designing primers to undisclosed regions of a nucleic acid encoding the *Arabidopsis* Met1 protein and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed in female germ line cells down-regulate one or more DNA methylating enzymes present in the plant and produce a plant whose seeds produce a modified endosperm.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

(10) Response to Arguments

Appellant's arguments and Examiner's response to the 112 2nd paragraph rejection

Appellant asserts one of ordinary skill would understand what is claimed based on basic tenets of molecular biology, i.e., the transcription product of an *Arabidopsis* Met1 sequence (or the *Z. mays* ortholog) is an RNA sequence that is a faithful copy of the DNA template from which the transcription product was transcribed (page 10 of Brief, 1st paragraph). Appellant asserts that previously cited references show that the designation *Arabidopsis* Met1 sequence

Art Unit: 1638

refers to the sequence of Accession No. L10692, which itself was derived from an RNA sequence (page 10 of Brief, 2nd paragraph). Appellant asserts that Finnegan et al., Nucleic Acids Res. 21:2383-2388 (1993) isolated RNA from *Arabidopsis* and created the cDNA sequence which is deposited as Accession No. L10692, and is 4720 bp (4.7kb) in length. Appellant asserts that one of ordinary skill in the art would immediately understand that the transcription product of Accession No. L10692 is an RNA that has the same sequence as L10692, with U substituted for T (page 10 of Brief, 4th paragraph).

The Examiner asserts that one of ordinary skill in the art would not be apprised of the explicit DNA sequence which Appellant is using in the claimed method. The Examiner asserts Appellant does not explicitly recite a DNA sequence in the claimed method that one of ordinary skill would immediately recognize. Appellant instead recites "a method comprising a sequence whose transcription product" is, for example, the *Arabidopsis* Met1 sequence. One skilled in the art knows transcription products are RNA molecules, but according to Appellant, the transcription product is a DNA sequence of Accession No L10692. The Examiner asserts, that not only would the transcription product be a RNA sequence, but the transcription product would be in a reverse orientation, because it would be the complement of the coding strand of the specified sequence. In addition, transcription products can also comprise sequences that will eventually be spliced out of the sequence, e.g., intron sequences and non-translated 5' and 3' regions, which are not disclosed in Accession No. L10692. Therefore, Appellant's statement "the designation *Arabidopsis* Met1 will always refer to the sequence of Accession No. L10692" does not make definite the recitation "a sequence whose transcription product comprises a partial or full length *Arabidopsis* (or *Zea mays*) DNA methyltransferase 1 (Met1) sequence".

Appellant's arguments and Examiner's response to the Written Description rejection

Appellant asserts that the Examiner acknowledged that the specification discloses a DNA sequence having accession number L10692 and that this sequence was known in the art (page 11 of Brief, 3rd paragraph).

The Examiner acknowledges the *Arabidopsis* Met1 sequence was known in the art prior to the filing date of the instant application but the instant application does not explicitly recite that the disclosed sequence is recited in the prior art as accession number L10692. The Examiner asserts the specific disclosure of the MET1 sequence as accession number L10692 was disclosed by Appellant in the remarks filed 2/25/2005.

Appellant asserts that the specification provides more than adequate written description for the *Arabidopsis* Met1 sequence to achieve targeted downregulation of DNA methylating enzymes and modification of endosperm (page 13 of Brief, top paragraph). Appellant asserts that the specification indicated that the Met1 gene can be used in antisense orientation to downregulate methylating enzymes in the plant (page 13 of Brief, 1st full paragraph). Appellant asserts the present specification discloses a working example using a partial Met1 sequence. Appellant asserts that Example 3 describes preparing a partial *Arabidopsis* Met1 antisense sequence and Example 4 describes its use to produce modified endosperm. Appellant cites pages 30-32, Examples 3-4 (page 13 of Brief, 3rd full paragraph).

The Examiner asserts that the claims are drawn to a method comprising a nucleic acid sequence whose transcription product comprises a *partial* or full-length *Arabidopsis* DNA methyltransferase 1 (Met1) sequence. Appellant does not disclose any sequence whose

Art Unit: 1638

transcription product comprises a *partial Arabidopsis* Met1 sequence that can be used to produce modified endosperm. The Examiner asserts pages 30-32 of the specification describe how to produce one sequence whose transcription product is the full length sequence of the *Arabidopsis* Met1 gene. Appellant's specification recites "The Met1 cDNA is 4.7 kb long and is isolated by RT-PCR from *Arabidopsis* cDNA using the primers MET1F and MET1R" (page 30 of specification, lines 23-24). The Examiner asserts Appellant's specification teaches making the pAGL5-asMET1 vector (see page 31 of specification, lines 1-2) whose transcription product is the full-length *Arabidopsis* Met1 sequence, as disclosed in accession number L10692, and is not a *partial* sequence. Therefore, Appellant does not disclose any partial sequence. In addition, Appellant does not disclose essential domains or any structural information which would permit one skilled in the art to identify and isolate partial sequences that can be used to downregulate one or more methylating enzymes and produce a plant whose seeds produce a modified endosperm.

Appellant asserts the *Arabidopsis* Met1 sequence was known in the art and cites as an example Finnegan et al., Nucleic Acids Res. 23:2383-2388 (1993). Appellant asserts the specification indicates that the *Arabidopsis* Met1 sequence is published as Accession No. L10692. Appellant asserts that the specification indicated that down regulation of Met1 can be achieved using full length or partial antisense Met1 sequences, or full length or partial sense Met1 sequences, or ribozymes directed against MET1 or combinations thereof (page 13 of Brief, 4th full paragraph). Appellant asserts that reciting actual partial *Arabidopsis* Met1 sequences in the specification is not necessary because one of ordinary skill in the art would easily visualize the identity of partial *Arabidopsis* Met1 sequences based on the full-length sequence (sentence

Art Unit: 1638

bridging pages 13-14 of Brief). Appellant asserts that partial or full-length *Arabidopsis* Met1 sequence is not new or unknown that one of ordinary skill would easily miscomprehend (page 14 of Brief, top paragraph).

The Examiner asserts that for claims drawn to a method comprising a sequence whose transcription product comprises a full length *Arabidopsis* Met1 sequence, Appellant has fulfilled the written description requirement. The Examiner asserts that for claims drawn to a method comprising a sequence whose transcription product comprises a partial *Arabidopsis* Met1 sequence, Appellant has not satisfied the written description requirement. Appellant has not disclosed any sequence whose transcription product comprises a partial *Arabidopsis* Met1 sequence and is effective for down-regulating one or more DNA methylating enzymes present in the plant. Appellant has not disclosed a representative number of partial sequences that can be used to down-regulate one or more methylating enzymes present in the plant and thereby produce a plant whose seeds have a modified endosperm. Appellant has not disclosed a structure function relation for any partial sequence that is operable in Appellant's claimed invention.

Appellant asserts the Examiner's interpretation of "partial" as comprising any dinucleotide is contrary to the evidence as disclosed in the 37 CFR §1.132 Declaration by Dr. Steven Jacobsen (page 14 of Brief, 1st and 2nd full paragraphs). Appellant asserts as stated in the Jacobsen Declaration, that one of ordinary skill in the art would not have interpreted a partial *Arabidopsis* Met1 sequence to comprise only two consecutive nucleotides because two nucleotides are too short to stably hybridize to a complementary sequence for downregulation to occur (page 14 of Brief, 3rd full paragraph). Appellant asserts that the Examiner did not fully consider the Jacobson Declaration (paragraph bridging pages 14-15 of Brief). Appellant asserts

Art Unit: 1638

that the Examiner's interpretation of "partial" is contrary to the standards of claim interpretation and that the Examiner is to give claims their broadest reasonable interpretation consistent with the specification, as they would be understood by one of ordinary skill in the art (page 15 of Brief, 1st full paragraph).

The Examiner asserts Appellant has not defined what nucleotides are required in a partial sequence to be operable in Appellant's claimed invention. The Examiner acknowledges that two nucleotides hybridizing to an endogenous sequence, may not be able to trigger a down-regulation of the endogenous gene and not produce the desired phenotype. But, Appellant has not disclosed any partial sequence for one of skill in the art to use in the claimed invention. Appellant has not disclosed a cut off of number of nucleotides that are required to operably hybridize to its target and achieve down-regulation of one or more methylating enzymes. Appellant has not disclosed any structural features common to members of the claimed genus that one skilled in the art can use to identify sequences that would work in Appellant's invention.

Appellant asserts the reliance on Lilly by the Examiner is misplaced because partial or full-length *Arabidopsis* Met1 sequences are not a new or unknown biological material (page 15 of Brief, 2nd full paragraph). Appellant asserts that Example 3 describes the construction of a female germ line specific vector, pAGL5-asMET1, containing a partial *Arabidopsis* Met1 antisense sequence and references page 30, line 21 to page 31, line 2 (page 16 of Brief, 1st paragraph). Appellant asserts that Example 4 describes *Arabidopsis* transformation with said vector and that data collected from the transgenic plants is presented on page 31, lines 18-28 and Table 1.

Art Unit: 1638

The Examiner asserts that the specification does not disclose a vector containing a *partial Arabidopsis* Met1 antisense sequence for the reasons stated above.

Appellant asserts that case law was recited in previous actions in arguing the written description requirement but the Examiner asserted that the fact pattern for the presented case law and the fact pattern for the instant application was not the same. Appellant asserts the issue is not whether the fact patterns are the same, the issue is whether Federal Circuit precedent is being followed (page 16 of Brief, 2nd and 3rd paragraphs). Appellant asserts merely because the fact patterns are not the same is insufficient basis to dismiss Capon and Falkner (sentence bridging pages 16-17 of Brief). Appellant asserts the complete *Arabidopsis* Met1 sequence was known from Accession No. L10692 and one of ordinary skill in the art would have easily comprehended the identity of partial *Arabidopsis* Met1 sequences based on the full-length sequence and one of ordinary skill in the art would not interpret partial sequences to comprise only two consecutive nucleotides. Appellant asserts a *per se* recitation of partial and full-length sequences within the specification is not required to satisfy the written description requirement (page 17 of Brief, top paragraph).

The Examiner asserts Appellant has not disclosed a structure function relationship which allows one skilled in the art to identify partial sequences that would be operable in Appellant's claimed invention. Appellant only discloses a full-length *Arabidopsis* Met1 antisense nucleic acid sequence. Appellant has not disclosed which partial sequence(s) can be used to effectively down-regulate one or more methylating enzymes present in the plant and produce a plant whose seeds produce a modified endosperm. Appellant has not disclosed which nucleotides of the *Arabidopsis* Met1 sequence can be used to down regulate methylating enzymes and produce a

Art Unit: 1638

plant whose seeds produce a modified endosperm. The state-of-the-art teaches that plant methyltransferases are not all the same. Finnegan et al (1998, Annu. Rev. Plant Physiol. Plant Mol. Biol. 49:223-247) states "There is evidence supporting the notion that plant methyltransferases may differ in target specificity" (page 229, bottom paragraph). The Examiner contends Appellant has not disclosed a representative number of partial Met1 sequences that can be used to down regulate one or more DNA methylating enzymes and produce a plant whose seeds have a modified endosperm. Therefore, the Examiner asserts Appellant is not in possession of the broadly claimed genus.

On pages 17-20 of the Appeal Brief, Appellant addresses particular claims, starting with claim 21. Only those issues which the Examiner believes have not been addressed above are summarized and addressed below.

Claim 82: Appellant has included an alignment between the *Arabidopsis* and *Zea mays* Met1 DNA sequences, Appendix E (page 20 of Brief, top paragraph). Appellant asserts that there are numerous regions that have greater than 75% identity. Appellant makes reference to nucleotides 731 to 856 which exhibit 76% identity, nucleotides 3329 to 3981 which exhibit 82% identity, nucleotides 3635 to 3720 which exhibit 91% identity, and nucleotides 4331 to 4590 which exhibit 82 % identity. Appellant asserts in view of the alignment, there is more than adequate written description for the use of monocot plants.

The Examiner asserts Appellant has not indicated which regions are specific to the methyltransferase of the instant invention. Finnegan et al (1998) discloses that there are three classes of methyltransferases in *Arabidopsis*, METI, METII and METIII (page 228, top

Art Unit: 1638

paragraph) and homology between METI and METII is higher in the methyltransferase domain than in the amino-terminal domain (sentence bridging pages 227-228). Finnegan et al (1998) states “There is evidence supporting the notion that plant methyltransferases may differ in target specificity” (page 229, bottom paragraph). Therefore, the Examiner asserts, Appellant has not described essential regions of the MET1 sequence that can be used to down regulate a methyltransferase in a plant so that the plant produces seeds with the expected phenotype. Appellant has not disclosed a structure function relationship for the sequences that produce the claimed phenotype. Therefore, given the lack of disclosure, Appellant is not in possession of partial *Arabidopsis* Met1 sequences that are effective for down-regulating one or more DNA methylating enzymes which results in plants whose seeds produce a modified endosperm.

On pages 21-27 of the Appeal Brief, Appellant addresses the written description rejection as it pertains to “a partial or full-length *Zea mays* ortholog of the *Arabidopsis* Met1 sequence”. Only those issues which The Examiner believes have not been addressed above are summarized and addressed below. The Examiner asserts that the arguments pertaining to *partial Arabidopsis* Met1 sequences (as stated above) are applicable to *partial Zea mays* sequences, and will not be repeated below.

Appellant asserts the *Z. mays* Met1 ortholog sequence was known in the art and that the carrot, *Arabidopsis*, pea and tomato Met1 sequences were known from the earliest priority date from Genbank Accession numbers AF063403, AF007807, L10692, AF034419 and AJ002140, respectively (page 21 of Brief, bottom paragraph). Appellant asserts there are numerous regions that are highly conserved even though *Zea mays* is a monocot and the remainder are dicots,

Art Unit: 1638

directing one of ordinary skill in the art to identify partial sequences that would be effective for downregulation in heterologous species.

The Examiner asserts that Appellant has not disclosed which regions of homology are specific to Met1 genes that when silenced, produce plants whose seeds produce a modified endosperm. Appellant has only pointed to known Met1 orthologous sequences of the *Arabidopsis* Met1 sequence. Appellant has not disclosed partial *Zea mays* Met1 sequences that are effective for downregulating one or more DNA methylating enzymes in a plant, wherein the plant produces seed with a modified endosperm. See also the above discussion.

Appellant's arguments and Examiner's response to the Enablement rejection

Appellant asserts the Examiner's interpretation of the word "partial" in the claims is contrary to the understanding of one of ordinary skill in the art as attested to by the Jacobsen Declaration (page 29 of Brief, item #1 and page 30, top paragraph). Appellant asserts that according to the Jacobsen Declaration, one of ordinary skill in the art would not have interpreted "partial" to mean a sequence comprising only 2 nucleotides as 2 nucleotides are too short to stably hybridize to a complementary sequence such that downregulation can occur (*Ibid*).

Appellant asserts that the Examiner's interpretation of "partial" is also contrary to the standards for claim interpretation during prosecution (page 30 of Brief, 3rd paragraph). Appellant asserts the Examiner's interpretation of "partial" is inconsistent with the specification, in view of the Jacobsen Declaration, given that the Examiner is to give claims their broadest reasonable

Art Unit: 1638

interpretation consistent with the specification, as they would be understood by one of ordinary skill in the art.

The Examiner asserts Appellant has not defined a “partial” *Arabidopsis* Met1 sequence that is effective for down-regulating one or more DNA methylating enzymes present in a plant. Appellant has only disclosed a construct comprising a full length *Arabidopsis* Met1 cDNA sequence that is operably linked to a female germ-line promoter wherein the sequence is in antisense orientation, and wherein introduction of said construct produces plants whose seeds produce a modified endosperm (see specification pages 30-32 of specification). Appellant has not disclosed a partial *Arabidopsis* Met1 sequence, nor has Appellant disclosed which regions of the *Arabidopsis* Met1 sequence can be used as a partial sequence to produce plants whose seeds produce a modified endosperm.

It is the position of the Office to give the claims their broadest reasonable interpretation. Appellant asserts that a sequence comprising any two nucleotides of the *Arabidopsis* Met1 sequence is not reasonable based on the Jacobsen Declaration. The Examiner asserts there is no clear definition, either in the specification or in the relevant art, of what constitutes a partial sequence. The Examiner interprets a partial sequence to be any sequence that is shorter than the 4.7 kb cDNA sequence to which Appellant is referring on page 30 of the specification, line 23. The Examiner asserts partial sequences include sequences of any length, including 2 nucleotides, given the lack of teaching as to the definition of “partial”. Therefore, given the state-of-the-art and unpredictability as stated above, and given the breadth of the claims, undue trial and error experimentation would be required by one skilled in the art to test thousands of “partial” sequences to find those, if any, that when transformed into a plant under conditions specified

Art Unit: 1638

above, will produce a plant whose seeds produce a modified endosperm. The Examiner asserts the claims are not enabled for “partial” sequences.

Appellant asserts that the Examiner’s interpretation that the claim does not specify that the promoter and the *Arabidopsis* Met1 sequence are operably linked is contrary to the interpretation that would have been given by one of ordinary skill in the art (page 30 of Brief, 4th paragraph). Appellant asserts that as indicated by the Jacobsen Declaration, one of ordinary skill would have interpreted the claim to mean that a promoter that targets expression to female germ line cells drives transcription of the indicated Met1 sequence. Appellant asserts that the plain language of the claim requires that the introduced nucleic acid is effective for down-regulating one or more DNA methylating enzymes in the plant. If the sequence is not operably linked to the female germ line promoter, then said sequence would not be effective for down-regulation (paragraph bridging pages 30-31 of Brief). Appellant asserts the Examiner stated limitations from the specification are not read into the claims. However, the Examiner has not indicated what limitation from the specification is being read into the claim (page 31 of Brief, 1st full paragraph).

The Examiner asserts that claim 20, for example, is drawn to a method comprising a nucleic acid molecule comprising a promoter that targets expression to female germ line cells “and” a sequence. The Examiner contends the recitation “and” does not automatically imply that the two sequences are operably linked to each other even though the specification discloses that for the claimed method, the promoter and MET1 cDNA are operably linked to each other. The Examiner asserts that the specification discloses a construct comprising the AGL5 promoter operably linked to the *Arabidopsis* Met1 cDNA in antisense orientation and said construct is

Art Unit: 1638

designated pAGL5-asMET1 (see figure 6 pages 30-31, Example 3). The Examiner asserts that one skilled in the art would understand that the AGL5 promoter is operably linked to the MET1 sequence in antisense orientation based on the notation “pAGL5-asMET1” and the diagram of said construct as illustrated in figure 6. The limitation to which the Examiner is referring is that the two sequences are operably linked to each other. The Examiner asserts that the claim does not specify that the two sequences are operably linked and it was the intention of the Examiner to use the enablement rejection to persuade Appellant to replace the recitation “and” with the recitation--operably linked--, for the reasons stated above.

Appellant asserts the Examiner’s requirement for detailed recitation of partial *Arabidopsis* Met1 sequences that have been empirically tested misplaces the focus of the enablement inquiry on the length of the disclosure rather than its substance (page 31 of Brief, 4th full paragraph). Appellant asserts that the Examiner’s assertion that ‘not all 3’ and 5’ regions will work’ is not enough to outweigh the evidence supporting enablement of the claim (page 32 of Brief, 1st full paragraph) Appellant asserts the *Arabidopsis* Met1 sequence is known from Accession number L10692 and that additional Met1 sequences from carrot, corn, pea and tomato were known from the earliest priority date from Genbank accession numbers and that an alignment of the sequences illustrates there are regions in the sequences that are highly conserved. Appellant asserts one of ordinary skill would be able to use this information to produce partial *Arabidopsis* Met1 sequences that would have been effective for downregulation in heterologous species. Appellant asserts methodologies for screening plants having partial sequences for decrease in the degree of overall DNA methylation were known and as stated in the Jacobsen Declaration, paragraph 23, “It is my opinion that one of ordinary skill would have expected that in general

Art Unit: 1638

heterologous partial or full length sequences can be used to downregulate endogenous genes based on, *inter alia*, the successful results reported in the references of paragraph 22”.

The Examiner asserts that the *Arabidopsis* MET1 sequence is essential to the presently claimed invention and was known in the prior art from Accession Number L10692, but said Accession Number is not disclosed by Appellant in the instant specification. The Examiner acknowledges that there are regions among the *Arabidopsis*, carrot, corn, pea and tomato Met1 sequences that are conserved, but Appellant has not disclosed which of these regions are specific to Met1 sequences of the instant invention that can be used to produce plants whose seeds produce a modified endosperm. Finnegan et al (1998) discloses that there are three classes of methyltransferases in *Arabidopsis*, METI, METII and METIII (page 228, top paragraph) and homology between METI and METII is higher in the methyltransferase domain than in the amino-terminal domain (sentence bridging pages 227-228). Finnegan et al (1998) states “There is evidence supporting the notion that plant methyltransferases may differ in target specificity” (page 229, bottom paragraph). Therefore, The Examiner asserts, Appellant has not taught which conserved regions can be used as a partial sequence in the instantly claimed invention; which regions are specific to methyltransferases that when down-regulated produce seeds with modified endosperm. Therefore, given the state-of-the-art and unpredictability as stated above, and given the breadth of the claims, undue trial and error experimentation would be required by one skilled in the art to test thousands of “partial” sequences to find those, if any, that when transformed into a plant under conditions specified above, will produce a plant whose seeds produce a modified endosperm. The Examiner asserts the claims are not enabled for “partial” sequences.

Art Unit: 1638

Appellant asserts that the Examiner has not responded to Appellant's remarks or to remarks made in the Jacobsen Declaration regarding the Fourgoux-Nicol article, even though the Examiner stated that the article is no longer applicable because the reason it was initially cited is no longer germane to prosecution (page 33 of Brief, 1st full paragraph). Appellant asserts the Examiner has ignored the aspects of Fourgoux-Nicol that are germane to prosecution, in particular, paragraphs 17-20 of the Jacobsen Declaration in which it is stated that the data from said reference indicates that the *Arabidopsis* Met1 sequence would hybridize to a heterologous sequence.

The Examiner asserts that the Fourgoux-Nicol reference deals with DNA-DNA hybridization reactions performed in a laboratory and is not related to RNA-RNA interactions taking place within a cell. Therefore, The Examiner asserts said reference is not germane to the instantly claimed invention because the instantly claimed invention is drawn to a sequence whose transcription product (RNA) is effective for down-regulating one or more methylating enzymes in plants (RNA-RNA) and produces modified endosperm in seeds.

Appellant asserts that the Examiner's position appears to be that since there is a failure to disclose "partial" sequences, claim 20 is not enabled despite Appellant's arguments and the Jacobsen Declaration (page 33 of Brief, 2nd full paragraph). Appellant asserts that the specification discloses partial sequences are useful and a working example in which a partial *Arabidopsis* Met1 sequence was used to produce modified endosperm is disclosed. Appellant points to page 30, lines 15-19 and pages 30-32, Examples 3-4 (page 33 of Brief, 3rd full paragraph).

Art Unit: 1638

The Examiner asserts that Appellant does disclose that partial sequences are useful, but no working example or reference is cited in which a partial sequence is actually used in Appellant's claimed invention. The Examiner asserts that the claims are drawn to a method comprising a nucleic acid sequence whose transcription product comprises a *partial* or full-length *Arabidopsis* DNA methyltransferase 1 (Met1) sequence. Appellant does not disclose any sequence whose transcription product comprises a *partial Arabidopsis* Met1 sequence that can be used to produce modified endosperm. The Examiner asserts pages 30-32 of the specification describe how to produce one sequence whose transcription product is the 'full length' sequence of the *Arabidopsis* Met1 gene. Appellant's specification recites "The Met1 cDNA is 4.7 kb long and is isolated by RT-PCR from *Arabidopsis* cDNA using the primers MET1F and MET1R" (page 30 of specification, lines 23-24). The Examiner asserts Appellant's specification teaches making the pAGL5-asMET1 vector (see page 31 of specification, lines 1-2) whose transcription product is the full-length *Arabidopsis* Met1 sequence, as disclosed in accession number L10692, and is not a *partial* sequence. Therefore, Appellant does not disclose any partial sequence.

Appellant asserts that in response to the Examiner's assertion that partial sequences are not disclosed, the Jacobsen Declaration referred to publications that show the use of heterologous sequences to downregulate an endogenous gene (page 33 of Brief, 4th paragraph).

The Examiner asserts the Jacobsen Declaration, in paragraph 21, recites four references which use antisense sequences to down-regulate gene expression. The Examiner asserts that three of the references use full length cDNA sequences and one reference uses a genomic sequence comprising 1.64 kb of genomic DNA which includes the first exon and 5' flanking

Art Unit: 1638

sequence. The Examiner asserts Appellant has not disclosed any partial sequences that can be used in the claimed invention.

Appellant asserts the Emery reference, which was cited by the Examiner, is a post filing date reference and is not relevant to whether the claimed invention would have been enabled as of the effective filing date (page 34 of Brief, top paragraph).

The Examiner asserts that Appellant's method is disclosed in the Emery et al reference because Appellant is relying on an antisense mechanism to produce the desired phenotype. According to the MPEP §2164.05(a) "In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513-14 (Fed. Cir. 1993) an article published 5 years after the filing date of the application adequately supported the examiner's position that the physiological activity of certain viruses was sufficiently unpredictable so that a person skilled in the art would not have believed that the success with one virus and one animal could be extrapolated successfully to all viruses with all living organisms". In the instant application, Appellant is relying on antisense technology to produce the desired phenotype and Emery et al state a 100% sequence match is required between the introduced sequence and its target.

The Jacobsen Declaration discloses that sequences having less than 100% sequence identity to an endogenous gene can be used for downregulation, see paragraphs 21-27 (page 33 of Brief, 4th paragraph). Appellant has submitted eight additional references that report downregulation using heterologous sequences, including sequences having less than 100% sequence identity to an endogenous gene (page 34 of Brief, top paragraph).

The Examiner asserts all eight references use full length sequences to down-regulate endogenous genes. The Examiner acknowledges full length sequences can be used in

Art Unit: 1638

heterologous systems. But, the Examiner asserts without a specific teaching as to which partial sequences are operable in the claimed invention, or which regions of the full length sequence are conserved in homologous sequences and are specific to the MET1 genus of sequences, and given the state-of-the-art and unpredictability as stated above, and given the breadth of the claims, undue trial and error experimentation would be required by one skilled in the art to test thousands of “partial” sequences to find those, if any, that when transformed into a plant under conditions specified above, will produce a plant whose seeds produce a modified endosperm. The Examiner asserts the claims are not enabled for “partial” sequences.

Appellant asserts that the Examiner misstated the facts by alleging that the specification does not disclose a partial *Arabidopsis* Met1 sequence that produces seeds with a modified endosperm. Appellant cites specific locations within the specification (page 34 of Brief, 2nd full paragraph).

The Examiner asserts pages 30-32 of the specification describe how to produce one sequence whose transcription product is the ‘full length’ sequence of the *Arabidopsis* Met1 gene. Appellant’s specification recites “The Met1 cDNA is 4.7 kb long and is isolated by RT-PCR from *Arabidopsis* cDNA using the primers MET1F and MET1R” (page 30 of specification, lines 23-24). The Examiner asserts Appellant’s specification teaches making the pAGL5-asMET1 vector (see page 31 of specification, lines 1-2) whose transcription product is the full-length *Arabidopsis* Met1 sequence, as disclosed in accession number L10692, and is not a *partial* sequence. Therefore, Appellant does not disclose any partial sequence.

Appellant asserts that the Jacobsen Declaration states that partial and full length *Arabidopsis* Met1 sequences could be expected to downregulate more than one endogenous

Art Unit: 1638

methyltransferase in non-*Arabidopsis* plants. Appellant continues by asserting that it is recognized that if one targeted expression of partial or full-length *Arabidopsis* Met1 sequences to the female germ line of a non-*Arabidopsis* plant, it does not matter for enablement whether more than one DNA methyltransferase is downregulated, and the Examiner has given no reason why it does matter to his enablement rejection (page 35 of Brief, top paragraph).

The Examiner asserts that the main enablement issue is the recitation of partial sequences to achieve the desired phenotype. The Examiner reiterates that Appellant has not disclosed any nucleic acid molecules comprising a nucleic acid sequence whose transcription product comprises a *partial Arabidopsis* DNA methyltransferase 1 sequence, wherein the introduced nucleic acid is effective for down-regulating one or more DNA methylating enzymes present in the plant. Appellant has only disclosed one *Arabidopsis* DNA methyltransferase 1 sequence that when transformed into a plant in an antisense orientation produce a plant whose seeds produce a modified endosperm. Given the state-of-the-art and unpredictability as stated above, and given the breadth of the claims, undue trial and error experimentation would be required by one skilled in the art to test thousands of “partial” sequences to find those, if any, that when transformed into a plant under conditions specified above, will produce a plant whose seeds produce a modified endosperm. The Examiner asserts the claims are not enabled for “partial” sequences.

On pages 35-39 of the Appeal Brief, Appellant addresses particular claims, starting with claim 21. Only those issues which The Examiner believes have not been addressed above are summarized and addressed below.

Claim 82: Appellant asserts the specification discusses techniques for transforming monocots and indicates at page 32, line 6-9, that the female germ line Met1 antisense vector, pAGL5Met1as, could be transformed into *Zea mays* (page 38 of Brief, 1st paragraph). Appellant asserts one of ordinary skill would have been aware that Met1 nucleotide sequences have a high degree of sequence identity and that there are regions that are highly conserved; see e.g., Finnegan et al., Ann. Rev. Plant Physiol. Plant Mol. Boil. 49:223-247 (1998), at pages 227-229. Appellant has included an alignment between the *Arabidopsis* and *Zea mays* Met1 DNA sequences, Appendix E (page 38 of Brief, top paragraph). Appellant asserts that there are numerous regions that have greater than 75% identity. Appellant makes reference to nucleotides 731 to 856 which exhibit 76% identity, nucleotides 3329 to 3981 which exhibit 82% identity, nucleotides 3635 to 3720 which exhibit 91% identity, and nucleotides 4331 to 4590 which exhibit 82 % identity. Appellant asserts in view of the alignment, there is more than adequate written description for the use of monocot plants. The Examiner asserts Appellant has only exemplified the pAGL5-Met1as construct in the dicot plant *Arabidopsis*. The Examiner asserts one of ordinary skill in the art would recognize that the recited construct, pAGL5-Met1as, uses the promoter from the *Arabidopsis* AGL5 gene, which in *Arabidopsis* directs expression mainly in female germ line cells. One of ordinary skill in the art would immediately recognize that said promoter has not been shown to be specific to female germ line cells in monocots, e.g., *Zea may*, and would require further experimentation to elucidate the regions, if any, of the AGL5 promoter that are important for directing expression in *Zea mays* female germ line cells.

In addition, the Examiner asserts Appellant has not indicated which conserved regions of the *Zea mays* Met1 gene are specific to the methyltransferase of the instant invention. Finnegan

Art Unit: 1638

et al (1998) discloses that there are three classes of methyltransferases in *Arabidopsis*, METI, METII and METIII (page 228, top paragraph) and homology between METI and METII is higher in the methyltransferase domain than in the amino-terminal domain (sentence bridging pages 227-228). Finnegan et al (1998) states “There is evidence supporting the notion that plant methyltransferases may differ in target specificity” (page 229, bottom paragraph). Therefore, The Examiner asserts, Appellant has not disclosed which regions of the *Zea mays* Met1 gene are essential and specific to MET1 that can be used as *partial* sequences to down regulate a methyltransferase in a plant so that the plant produces seeds with the expected phenotype. Therefore, the Examiner asserts, given the state-of-the-art and unpredictability as stated above, and given the breadth of the claims, undue trial and error experimentation would be required by one of skill in the art to practice the broadly claimed invention.

On pages 39-47 of the Appeal Brief, Appellant addresses the enablement rejection as it pertains to “a partial or full-length *Zea mays* ortholog of the *Arabidopsis* Met1 sequence”. The Examiner asserts *partial Zea mays* sequences have not been exemplified or disclosed; as stated for *partial Arabidopsis* Met1 sequences. Only those issues which the Examiner believes have not been addressed above are summarized and addressed below.

Appellant asserts that the specification discloses partial *Zea mays* orthologous sequences that can be used in the claimed method (page 44 of Brief, 2nd full paragraph). Appellant discloses specific locations within the specification which purportedly teach partial sequences.

The Examiner asserts that Appellant’s specification does not disclose any partial *Zea mays* Met1 orthologous sequences that can be used in the claimed methods. The Examiner

Art Unit: 1638

asserts none of the specified locations within the specification teach any partial *Zea mays* orthologous sequence. The specification merely states that orthologous sequences can be used, including AGL5 orthologous promoter sequences (see page 32 of specification, lines 6-8, as specified by Appellant).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Stuart F. Baum". The signature is fluid and cursive, with the first name "Stuart" and last name "Baum" clearly distinguishable.

Stuart F. Baum
Primary Examiner
Art Unit 1638

/Anne Marie Grunberg/
Anne Marie Grunberg
Supervisory Patent Examiner
Art Unit 1638

/Robert A. Wax/
Robert A. Wax
TQAS Appeals Specialist
TC 1600